



Impact of school-based educational interventions in middle adolescent populations (15-17yrs) on human papillomavirus (HPV) vaccination uptake and perceptions/knowledge of HPV and its associated cancers: a systematic review

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Background:

Human papillomavirus (HPV) infection is the most common sexually transmitted infection of the reproductive tract^{1,2} with the highest incidence occurring among teenagers and young adults^{3,4}. HPV types 16 and 18 are associated with approximately 70% of cervical cancers^{5,6,7} and HPV is also associated with penile cancer in males alongside cancers of the anus and oesophagus in both women and men^{6,8,9}. It is predicted that HPV-positive oropharyngeal cancer will soon become the most common HPV-associated cancer in the US with most cases occurring in males¹⁰.

Prophylactic HPV vaccines have been available for females for protection against HPV-associated cervical cancer since 2006¹¹ with many countries also introducing vaccination programmes for males in recent years¹². Merck's 9-valent HPV vaccine has the potential to prevent 90% of cervical, vulvar, vaginal, and anal cancers¹².

Despite the implementation of HPV vaccination programmes in a growing number of countries, there is a huge disparity in the uptake of the vaccination worldwide with the UK having one of the highest uptakes and the US having one of the lowest rates of uptake⁹. Recently, some countries have seen uptake of the HPV vaccination fall due to safety concerns. For example, Denmark achieved initial vaccination rates of 80-90%¹³, however, following escalation of public concern about possible side effects, based primarily on social and televised media information, this rate dropped to 23% in 2016¹⁴ recovering to 46% by 2017¹⁵. In 2013, Japan's health ministry also decided to withhold its recommendation of the HPV vaccination because of public concerns¹⁵. Ireland also experienced a significant fall in vaccination uptake after initially achieving high levels when a patient advocacy group raised concerns about side-effects in adolescent females^{14,15}. Despite safety concerns being addressed and dispelled¹⁶, this fluctuation highlights the importance of continuous re-enforcement of education regarding HPV vaccination to optimise vaccination uptake and improve HPV education in young people.

School-based education programmes have been very effective in producing significant positive changes in HPV knowledge and sexual behavior intentions^{9,17-19} though they typically involve 9-13 year old adolescents. As a consequence of this young age, educational HPV programmes have tended to focus on educating parents rather than students as parents are usually the primary decision-makers in this process for this age group²⁰⁻²⁴. Unfortunately, parents and education providers are often uncomfortable discussing sexual practices of adolescents²⁵ and are often concerned that HPV vaccines increase sexual activity among adolescents although there is no evidence to support this notion^{5,26}. Consequently, the majority of adolescents who receive the vaccination have low awareness and knowledge about the HPV virus, especially regarding cancer risks²⁷. Lack of parental acceptance of HPV vaccinations has been identified as being one of the main barriers of higher vaccine uptake^{28,29}.

Numerous countries report the average age of first sexual intercourse to be between 15-17 years old including the UK, France, Sweden, Nigeria, the US, Canada and Australia^{24,30-36} and therefore providing information regarding HPV risk is most relevant at this age, where adolescents are fundamentally more involved in decisions about their health and sexual practices^{9,37}. Many economically developed countries, while providing the HPV vaccination, do not have national school-based programmes embedded in their curricula and therefore little information is provided regarding HPV at any point in the national school curriculum^{38,39,40}. Consequently, it is estimated that adolescents 15-19 years old, still acquire 50% of all new STIs^{36,41} and are at the highest risk of contracting the HPV virus^{18,42}.

The aim of this systematic review is to assess the impact of school-based education interventions on HPV uptake and perceptions/knowledge of HPV and its associated cancers in 15-17 year old adolescents.

Methodology:

This systematic review was reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and a protocol was registered with PROSPERO prior to the commencement of the review⁴³. The search strategy, inclusion and exclusion criteria, study selection approach, evaluation of the quality of the studies, and data extraction process are described below.

Search strategy:

We conducted systematic searches of the following databases: Medline, EMBASE, Scopus, CINAHL, PsycInfo, PsycArticles, AMED and Cochrane Reviews. The PICO mnemonic - Population, Intervention, Comparison intervention, and Outcome measures - was used to establish search terms. The search strategy was based on using combinations of the following keywords and related index words: humanpapilloma virus; adolescent; uptake/education and randomised controlled trials/quasi-experiments/intervention. Although randomised controlled trials (RCTs) are the gold standard for inclusion in systematic reviews, the reviewers acknowledged that random assignment can be difficult or impossible in educational interventions⁴⁴ and therefore included both RCTs and quasi-experimental design studies (QEDs) in this review.

Inclusion and Exclusion Criteria:

RCTs and QEDs were included where a school-based educational intervention was implemented which included any adolescents between the ages of 15-17 years and the measured outcome was at least one of the following: HPV vaccination uptake, knowledge of HPV and associated cancers or perception/attitude regarding self-protection against HPV.

Potentially eligible studies were screened by title and abstract to assess whether they met the inclusion criteria. As licensure of the first HPV vaccine was established in 2006, studies prior to 2007 were not included. Studies were retrieved until the end of 2019. Figure 1 demonstrates the process of this review; AMED and Cochrane review yielded no results from the search and therefore were not added to the flow diagram.

Full-text articles were excluded where the study population was either college/university students over 17 years or alternatively students who were 11-14 years old. One potentially eligible study was excluded due to its unavailability in English⁴⁵. Another study was excluded as it was presented as a poster, lacking adequate detail to establish the quality of the study⁴⁶.

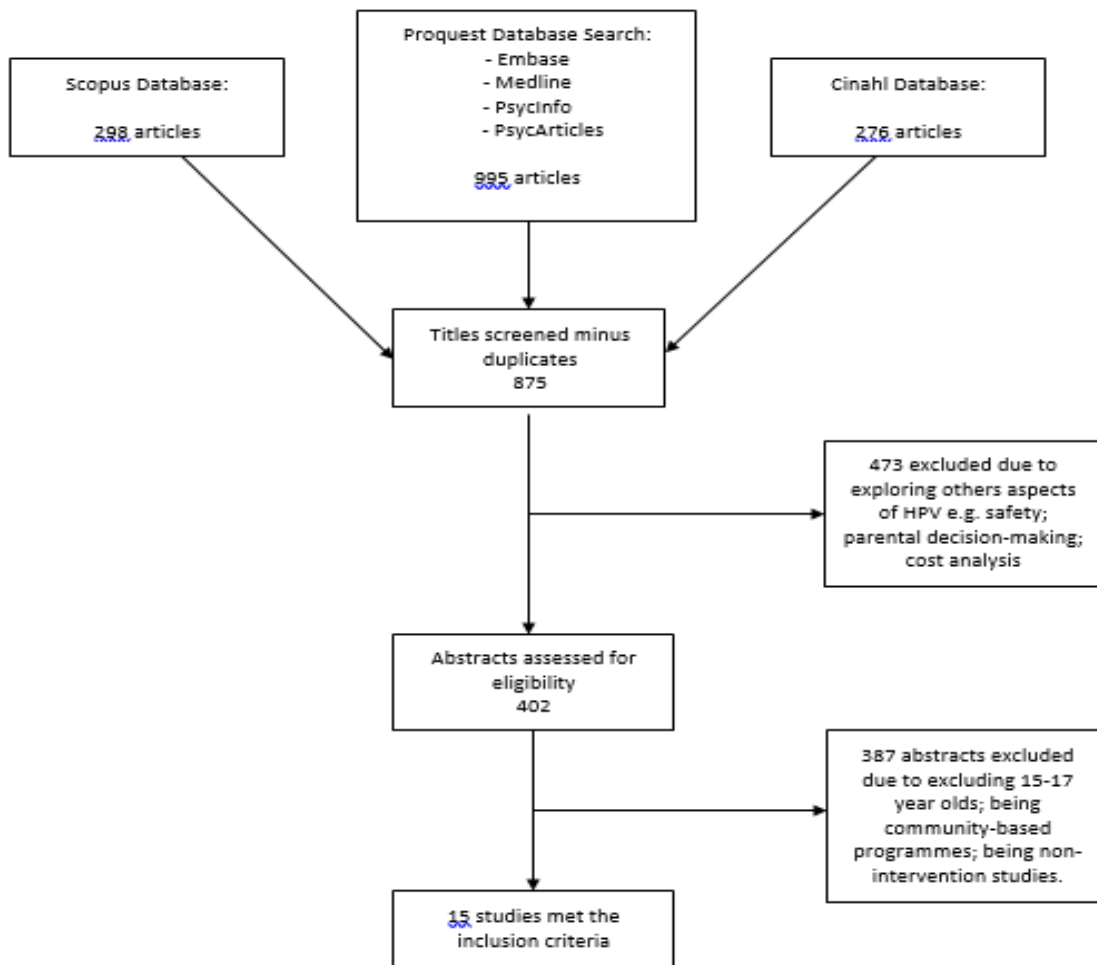


Figure 1 : Database search

Evaluation of the quality of the studies and data extraction process:

For each eligible article, we systematically extracted data, based on an agreed-upon set of categories (by consensus of all authors). These categories included bibliographic information, study design, aims of study, study population, theory of intervention, intervention design, data collection timeline and statistically significant measured outcomes of the intervention (summarized in Table 1).

The 'Quality Assessment Tool for Quantitative Studies' (QATQS) was used to assess the quality of the eligible articles. This instrument is widely established for use in the assessment of studies for systematic reviews related to sexual health, especially in the evaluation of public health programmes^{47,48}. Its content and construct validity are well-established, consisting of 8 standardized criteria scored on a 3-point scale corresponding to weak, moderate or strong with strong being the highest performing score⁴⁹. Two researchers independently scored each paper and consensus was reached within the research team where discrepancies occurred in the scoring.

	Selection bias	Study Design	Confounders	Blinding	Data Collection Methods	Withdrawal and dropout	Intervention Integrity	Analysis Appropriate to Question	Total Rating (Score out of 16)
Ali et al.	Moderate	Moderate	Moderate	Weak	Strong	Moderate	Weak	Strong	Moderate (8)
Sadoh et al.	Weak	Moderate	Strong	Weak	Moderate	Strong	Weak	Strong	Moderate (8)
Ifediora et al.	Moderate	Moderate	Weak	Weak	Moderate	Strong	Weak	Moderate	Moderate (6)
Davies et al.	Strong	Strong	Strong	Strong	Moderate	Weak	Strong	Strong	Strong (13)
Lim et al.	Moderate	Moderate	Weak	Weak	Weak	Moderate	Weak	Strong	Weak (5)
Yoost et al.	Weak	Moderate	Strong	Strong	Weak	Moderate	Strong	Strong	Moderate (10)
Grandahl et al.	Strong	Strong	Moderate	Weak	Strong	Strong	Strong	Strong	Strong (13)
Lai et al.	Moderate	Moderate	Strong	Weak	Strong	Weak	Moderate	Strong	Moderate (9)
Gargano et al.	Moderate	Moderate	Weak	Weak	Moderate	Weak	Strong	Strong	Moderate (7)
Steckelberg et al.	Moderate	Strong	Moderate	Strong	Moderate	Strong	Moderate	Strong	Strong (12)
Marek et al.	Moderate	Strong	Strong	Weak	Moderate	Strong	Moderate	Strong	Strong (11)
Merzouk et al.	Moderate	Moderate	Weak	Weak	Moderate	Moderate	Weak	Strong	Moderate (6)
Kwan et al.	Moderate	Moderate	Moderate	Weak	Moderate	Strong	Moderate	Strong	Moderate (9)
Gottvall et al.	Moderate	Strong	Moderate	Moderate	Strong	Moderate	Strong	Strong	Strong (12)
Lloyd et al.	Moderate	Moderate	Weak	Weak	Moderate	Strong	Moderate	Strong	Moderate (8)

Table 2: Quality Assessment Tool for Quantitative Studies rating for eligible studies. 'Strong' was allocated a score of two. 'Moderate' a score of one. 'Weak' a score of zero. [Studies were referred to as strong if score > 10, Moderate 6-10 and Weak ≤ 5]

Results:

Study Characteristics:

Our search yielded 15 school-based educational interventional studies of which 4 were RCTs and the remaining 11 studies were QEDs. Individual study quality was evaluated using the QATQS^{47,48}, with 5 out of 15 studies being rated to be of high quality, 9 studies rated as being of moderate quality and the remaining 1 study rated as being of poor quality (see Table 2). Blinding was generally considered the lowest ranking criteria as a study was deemed 'weak' where blinding was not described. Confounders were also considered 'weak' where control and intervention group demographics were not clarified. Where withdrawal and dropout were not discussed, the study also received a 'weak' grading.

Population profiles:

The 15 studies were conducted in a diverse range of countries including 3 from the US^{22,50,51}, 2 from Sweden^{3,52}, 2 from Nigeria^{53,54}, 1 from Germany⁵⁵, 1 from Hungary³⁸, 1 from Australia⁸ and 1 from the UK⁵⁶. The remaining 4 studies were from Asia including Singapore⁵⁷, Taiwan²⁸, Hong Kong³⁷ and Malaysia⁵⁸. Study sizes ranged considerably with the largest being Davies et al's⁸ study which included 6,965 students while Yoost et al.⁵¹ conducted a study with only 21 students completing all aspects of the study.

Outcome measures of Studies:

Post-intervention, all fifteen studies reported a statistically significant improvement in their specific outcome measures including changes in knowledge, attitude and perception with regard to HPV vaccination and associated cancer prevention. All of the studies aimed to improve knowledge related to HPV risk and HPV vaccination while many focused on improving positive attitudes/perceptions regarding self-protection against acquisition of HPV^{3,8,22,28,37,38, 51,52,57,58}.

Only 3 of the fifteen studies explored the actual effect of the intervention on HPV vaccination uptake^{3,8,51}. Two of these studies by Davies et al.⁸ and Grandahl et al.³, were large, high quality studies, including males and females, whose RCT designs were based on established scientific theories. However, while Grandahl et al.³ found that HPV vaccination uptake rates increased to a higher degree in the intervention group, Davies et al.⁸ did not find any difference between their intervention and control groups. Davies et al.⁸ proposed that, due to the HPV vaccination coverage being so high in both groups (>85% uptake), this finding could be related to a possible ceiling effect. In contrast to this, Grandahl et al.³ pre-intervention vaccination rate was only 52.5%, increasing to 59% after the intervention. Yoost et al.⁵¹, using a pre-test/post-test quasi-experimental design, found HPV vaccine initiation or completion was 38% at the time of the session post-test. This report increased to 71.4% at 6 months among those who attended that session.

Six additional studies recorded 'intention to be vaccinated' against HPV after the intervention^{22,28,37,38,56,57}. Four of the fifteen studies^{3,8,51,52} explored the impact of the intervention on sexual behavior intention including condom use. Nine of the studies also specifically aimed to improve cervical cancer prevention, knowledge and attitude^{28,37,38,52-54,56-58}.

Age Range:

All of the studies included adolescents between the ages of 15-17 years old. However, nine studies included adolescents ≤ 14 years old as well as middle adolescents ≥ 15 years old^{8,22,37,38,50,51,54,56,58}. Sadoh et al.⁵⁴ and Gargano et al.'s²² studies included the largest age ranges with students being between 9-17 years old and 11-18 years old respectively, with the same intervention being given to all students. Kwan et al.³⁷ included students 12-17 years old also providing the same intervention for all students.

Only two of the studies^{54,58} analysed differences in outcome measures in terms of age range. Sadoh et al.⁵⁴, indicated that there were no statistically significant differences in the mean scores between different ages before or after the intervention though age-specific baseline scores are not presented. However, Ali et al.'s⁵⁸ study found significantly improved knowledge in 16-year-old students compared to 13-14 years old students at baseline. Post-intervention, all students increased their knowledge significantly.

Data Collection:

Thirteen of the fifteen studies conducted a pre-intervention questionnaire to establish baseline knowledge of HPV and associated cancers in the control and intervention group. Davies et al.⁸ provided

a baseline questionnaire to the control group only and Lloyd et al.⁵⁶ did not include any baseline questionnaire.

Ten of the studies provided a post-intervention questionnaire directly after the intervention while seven studies captured information regarding attrition of knowledge at later time periods^{3,8,28,38,51,53,58} up to a maximum of 6 months^{8,51,53,58}.

Gender Inclusion

Nine of the fifteen studies included females only while five included both genders^{3,8,38,52,58} in their target populations. Merzouk et al.⁵⁰ did not state the gender of the population though the intervention assessment questions would imply that the population was female only.

Development and Design of Interventions

Significant variability was found in the design and content of the interventions in the studies. Psychological research has demonstrated that behaviours and behaviour change follow a predictable pattern and increasing evidence suggests that health-promotion interventions to affect behaviours are more effective when grounded in evidenced theory⁵⁹. Glanz and Bishop's article⁵⁹ summarises a number of behavioural science theories used for development and implementation of health promotion interventions including the Health Belief Model (HBM), The Theory of Reasoned Action (TRA) and Social Cognitive Theory (SCT)⁵⁹.

Five studies^{3,8,22,28,52} utilized concepts from the HBM to guide their teaching structure. Grandahl et al.³ and Gargano et al.²² also incorporated aspects of the TRA in the formation of their intervention. Gargano et al.²² also conducted a series of focus groups with middle- and high-school students, parents, and teachers to inform intervention structure and content. Davies et al.⁸, along with utilizing the HBM, also incorporated aspects of the Biopsychosocial Model and constructs of the Theory of Planned Behavior and SCT. This study additionally included a diverse range of stakeholder input in the creation of their programme. These 5 studies subsequently developed the most sophisticated and engaging interventions yielding statistically significant outcomes in terms of improved knowledge and attitude towards HPV vaccination. For example, Davies et al.'s⁸ intervention included an interactive lesson, take-home magazine, DVD with guide, app and website educational resources with relaxation methods to help increase the student comfort with the topic. Collectively, this study included 18 different teaching resources with guides to improve consistency in the intervention. Gargano et al.²² also utilized a combination of activities in their intervention including interactive games, projects, hands-on activities and powerful imagery in addition to utilizing colourful and animated PowerPoint slides. As with Davies et al.'s⁸ study, teaching guides were also created to improve consistency in the educational intervention.

Grandahl et al.³, Davies et al.⁸ and Gottvall et al.⁵², while covering the aforementioned topics, also included education around sexual behavior, condom use and various transmission routes of infection. Gottvall et al.'s⁵² intervention even involved practical teaching about how to use condoms. These 3 studies, which are all considered of high quality, included both females and males. These 3 studies also yielded statistically significant outcomes in terms of future sexual behavioural intentions.

Other models or theories utilized through the studies included the Theory of Persuasion³⁷ and a thematic analysis based on Leventhal's Common Sense Model of lay illness representations⁶⁰.

However, eight of the studies^{38,50,51,53-55,57,58} did not provide any details of theoretical models that they used to guide them in the planning and development of their educational intervention. Their interventions were generally simplistic in nature with a brochure/pamphlet only^{55,58}, DVD only⁵⁰ or a didactic presentation with a brochure/pamphlet^{53,54,57} or without a brochure/pamphlet³⁸.

Intervention format/delivery

The time required to deliver each educational intervention ranged from 10 minutes⁵⁷ to 120 minutes²². In most cases, the intervention was delivered by a professional with a nursing, healthcare or medical background^{3,28,37,38,51,52,54,57}. Only 3 studies included active interventions which were conducted by school health and social care teachers or science teachers^{8,22,50}. One study involved an intervention conducted by a teacher with a nursing background²⁸. See Table 1 for full details of each intervention.

Despite the variability in the intervention length and design, all studies (even those with short simple designs) demonstrated improved participant knowledge of HPV vaccination, HPV and it's associated cancers after any intervention.

Discussion

This literature review of 15 studies on interventions to improve HPV uptake, vaccination intentions, or attitudes among middle adolescents across the globe, demonstrates both the impact of interventions in this important demographic as well as potential novel directions for future work.

As previously established, only three of the fifteen studies explored the actual effect of the intervention on HPV vaccination uptake^{3,8,51}. Combined findings from Davies et al.⁸ and Grandahl et al's.³ large high quality studies and Yoost et al's⁵¹ smaller study, demonstrate the potential to increase HPV vaccination uptake rates in middle adolescent populations through school-based interventions, especially in countries where the initial vaccination uptake is quite low. Although a number of studies measured intention to be vaccinated^{22,28,37,38,56,57}, previous studies have demonstrated inconsistencies between intention to vaccinate and actual vaccination^{61,62} making 'intention' an unreliable predictor of uptake. With only three studies exploring the actual impact of educational interventions in middle adolescent populations, there is a need for further research in to this area.

Perhaps the most important aspect of this topic is the issue of self-consent. Introducing gender and age-appropriate information to 15-17 year old students provides them with the opportunity to self-consent to HPV vaccinations without the need for consent from their parents in many countries including the UK, Canada, Sweden and parts of the US^{23,24,63,64}. Unsurprisingly, the HPV vaccine can create ethical challenges for schools where there is some reticence about vaccinating without written parental consent^{23,24,63}. This is an important opportunity for middle adolescents to make personal and private decisions about their future health and wellbeing, which may not necessarily align with their parents' viewpoint regarding this vaccine. It is, therefore, also important that students are provided with

information regarding how they can access the HPV vaccination if they choose to have the vaccination at this time.

A variety of interventions were used through the 15 studies, with Davies et al.⁸ and Gargano et al.²² including a vast array of stakeholder input in to the design of their interventions alongside sound supporting scientific theory. These two studies resulted in the most diverse and engaging interventions. Gargano et al.²², with stakeholder engagement, designed the same intervention for all students ranging in age from 11 – 18 years of age. However, they did not acknowledge this as being a limitation of their study. Davies et al.'s⁸ intervention was designed for young adolescents at the time of initial vaccination rather than for middle adolescents. While a wide range of development and behaviour for each age is normal, certain attitudes, behaviours, and physical characteristics tend to occur at specific ages^{65,66}. Adolescence is a time of constant transition where major developments related to sexuality takes place⁶⁷ resulting in unique information needs at different ages in the adolescent spectrum. It is, therefore, paramount, that interventions are specifically designed to address the needs and interests of middle adolescents who have priorities that are different to their younger counterparts. Additionally, it is essential that this population play a key role in informing the creation of any proposed future intervention for this group.

Intervention Benefits

The content of the interventions largely focused on cervical cancer with only five of the fifteen studies including both genders^{3,8,38,52,58} and no studies including males only. Even where both genders were included, the information tended to focus on cervical cancer with little discussion around oropharyngeal cancer, which has now become one of the leading HPV associated cancers globally with men having a 3-4 fold increase in risk compared to women⁶⁸. Many adolescents who have not had vaginal intercourse, have engaged in sexual activity in the form of oral sex⁶⁹⁻⁷¹ but are unaware that HPV can be transmitted via this route⁷². Only a small number of studies^{3,8,51,52} really encouraged the use of open dialogue around the important issues relating to sexual behavior and HPV risk. Education at this time point should discuss the risks of acquiring HPV infections through vaginal, oral and anal sex along with prevention strategies to avoid infection. Where both genders were included in the study, the depth of discussion seemed to broaden to include wider discussion around sexual behavior and HPV prevention. Researchers who included males may be more likely to be passionate about ensuring that the risks of oropharyngeal, penile and anal cancer are understood in both male and female adolescents.

In the eligible studies, the education intervention session was taught by a variety of professionals including teachers^{8,22,50}, healthcare professionals^{3,28,37,51} and the research team, who primarily had a healthcare background^{38,52,54,57}. However, a recent review by Pound et al.⁷³, found that students often described their sexual education lessons with teachers as being clinical, with teachers often embarrassed to discuss issues like oral sex, and students equally reluctant to open up about private matters to their teachers. For this reason, the concept of peer education is an interesting one, though this was only explored in one isolated study⁵⁴. Whilst a huge increase in understanding and knowledge was observed after this peer teaching intervention, the knowledge gain was significantly less than the standard education in this study. This may be due to the lack of training provided to students to teach their peers, as the format of the peer teaching can have a large effect on the impact of the teaching⁷⁴. This format may well be worth exploring in the future as students reported feeling 'a sense of affinity' with their peers, encouraging them to believe information delivered by peer educators⁵⁴. Previous

findings have also indicated that peer training can increase knowledge and enhance preventive behaviors regarding sexually transmitted diseases (STDs)^{75,76}. Further research directed at exploring the value of peer-teaching for HPV education in teenagers would be beneficial in the future.

One of the common concerns from schools is the time and resources required to implement an educational strategy of this nature⁵⁰. However, this review demonstrates that even a short educational intervention with few resources can have a significant impact on knowledge gained and increase positive attitudes to safe sex and HPV vaccination. This intervention is even more important in countries where there is a cost associated with the HPV vaccine as these countries typically have lower vaccination rates⁹.

Intervention Frequency

A number of studies measured their outcomes at various time-points up to 6 months post-intervention^{3,8,28,38,51,53,58}. Their findings suggest that altered intentions and retention of information from the intervention, remains up to approximately 6 months post-intervention. After this time, small reductions in retention were observed, though they were still much higher than at baseline^{8,51,58}. This may suggest the need for short annual refresher interventions, specifically designed for middle adolescents, to obtain optimal impact, supporting the findings of previous studies^{38,77}. Studies need to follow-up students for longer periods post-intervention in order to verify this theory. Longer follow-up is also needed to understand whether intention translates in to real-lived behaviors including an increase in the uptake of HPV vaccination, cervical screening and increased condom use; all ways to reduce the incidence of HPV associated cancers^{78,79}.

Conclusion

This literature review provides evidence that implementation of educational interventions improves HPV uptake, vaccination intentions, and attitudes among middle adolescents globally. Currently, there is no evidence that any form of standard HPV education is being provided by schools to middle adolescents who are most likely to understand the relevance of this information and potentially adapt their future health and sexual practice behaviours as a result of this education. HPV vaccinations should be offered in conjunction with both an initial educational intervention and annual follow-up interventions for middle adolescents, to maximize vaccination uptake. These interventions, with information regarding associated cancers, should be a mandated school-based intervention, adapted to this specific age group and mixed genders. Interventions need to be sensitively constructed with input from students, teachers and the community outside of the school environment¹⁹. Some standardization of outcome measures used to capture information related to knowledge, attitude and intention to vaccinate is needed as there is currently a wide variety of tools used in the published research to assess these parameters. A theoretical foundation is becoming almost mandatory in the development of health education, as we are primarily interested in predicting and understanding patterns of behaviours in specific populations⁸⁰. This review supports the incorporation of behavioural science theories in the development of multimodal HPV related education for this population, as this results in a robust and engaging practical approach to education delivery^{8,22,52}.

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Bibliographic Information	Study design	Aims of study	Study Population	Theory of intervention	Intervention Design	Data Collection Timeline	Statistically Significant Measured Outcomes
Ali et al. 2018 (Malaysia)	Quasi-experimental Pre-test/Post-test with 1 group only	1. Assess Knowledge, Attitude and Perception (KAP) level changes among HPV vaccinated secondary school adolescents pre and post an educational intervention. 2. Estimate the impact of the educational intervention on KAP over time.	<i>Age:</i> 13,14 and 16 <i>Gender:</i> Males and females included <i>Numbers:</i> 2,928 appear to have completed the 3 questionnaires (HPV vaccination secondary school students who received at least the 1 st vaccination dose.)	Not discussed. (Health Belief Model mentioned but no indication that it was utilized in the design of the intervention.)	<i>Intervention:</i> Educational pamphlet containing information related to HPV infection, cervical cancer, its screening and HPV vaccination. There is no indication of who provided the class with the pamphlet and no evidence to suggest Q&A opportunity. The pamphlet could have been read anywhere and at any time. There is no way of establishing whether all students read the pamphlet .	A baseline questionnaire was completed prior to the intervention. A second questionnaire was completed 2 weeks after intervention. A third questionnaire was completed between 3-6 months post-intervention.	1. Knowledge, attitude and perception all improved significantly 2 weeks after the intervention. 2. 3-6 months post-intervention, KAP scores had fallen but were still significantly higher than at baseline.

<p>Sadoh et al. 2018</p> <p>(Nigeria)</p>	<p>Quasi-experimental Pre-test/Post-test with 2 groups</p>	<p>1. To assess the knowledge of female secondary school students about cervical cancer and HPV risk</p> <p>2. To determine if their knowledge could be improved using peer-to-peer transfer of knowledge.</p>	<p><i>Age:</i> 9-17 years old</p> <p><i>Gender:</i> Female only</p> <p><i>Numbers:</i> 1337 students (from 4 schools) completed baseline questionnaire.</p> <p>Following peer training, 1201 students completed post intervention questionnaire.</p>	<p>Not discussed</p>	<p>Arm 1 (Intervention 1; seminar cohort): 124 students participated in a training seminar involving a lecture with a brochure. (Length of seminar not specified)</p> <p>Arm 2: (Intervention 2; school cohort): 1,337 students participated in Peer-teaching using a brochure as the basis of discussion (length of discussion or Q&A opportunities not discussed)</p>	<p>A baseline questionnaire was completed by all students prior to intervention 1 or intervention 2.</p> <p>A second post-intervention questionnaire was completed by the seminar cohort immediately after the training while for those in the school cohort, the questionnaire was collected within 3–5 days after peer training.</p>	<p>1. Low awareness of cervical cancer prior to any intervention (~14.5% had ever heard of cervical cancer)</p> <p>2. There was no difference in the mean knowledge score between different ages at baseline.</p> <p>3. Sizable increase in understanding the link between sexual practices and HPV to cervical cancer after the intervention ($p < 0.0001$).</p> <p>4. The mean knowledge score for the seminar cohort post-training was higher than that of the school cohort though both were $> 80\%$ ($p < 0.0001$).</p> <p>5. There was no statistically significant difference in the mean scores between</p>
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							classes ($p = 0.68$) and between ages ($p = 0.27$) in seminar cohort following training. Following peer training there was no significant difference in the mean scores between classes ($p = 0.26$) and between different ages ($p = 0.60$) in the school cohort.
Ifediora et al. 2018 (Nigeria)	Quasi-experimental 2-armed study	<p>1) To assess the effect of an intervention on knowledge regarding Pap Smears, HPV vaccines and associated risk factors</p> <p>2) To assess the level of engagement of students in the two intervention options.</p>	<p><i>Age:</i> 15-19 years (>90%)</p> <p><i>Gender:</i> Females only</p> <p><i>Numbers:</i> 317 (73.4%) and 301 (69.7%) valid responses were received from the pre-intervention and post-intervention surveys from 24 schools.</p>	Not discussed	<p>Arm 1 (Intervention): Voluntary attendance at 45-minute PowerPoint-assisted lecture. Unclear who delivered the presentation or whether Q&A opportunity.</p> <p>All participants received a brochure with the same content as the powerpoint.</p>	<p>A baseline questionnaire was completed by both groups prior to the intervention.</p> <p>A second post-intervention questionnaire was completed 6 months after the intervention.</p>	<p>1. Significant improvements in knowledge across all parameters (Pap Smears, HPV Vaccines and Risk Factors) except on 'early symptoms' in intervention group.</p> <p>2. Of the 301 post-intervention respondents, 133 (44.2%) attended the symposium, while a total of 189 (62.8%) read the handouts (including some who</p>

					Arm 2 (control): No intervention		did not attend the symposium).
Davies et al. 2017 (Australia)	2-armed Cluster RCT	<p>1. To improve student knowledge about HPV vaccination</p> <p>2. To improve psycho-social outcomes including attitudes to HPV.</p> <p>3. To improve HPV vaccination uptake.</p>	<p><i>Age:</i> 13-15</p> <p><i>Gender:</i> Males and Females</p> <p><i>Numbers:</i> 40 schools with 6,965 students recruited.</p>	<p>-Biopsychosocial model</p> <p>-Health Belief model (HBM)</p> <p>-The Theory of Planned Behaviour and Social Cognitive Theory.</p>	<p>Arm 1 (intervention): Delivered by mainly Health and Social teachers with small groups structure. Average 60 minutes though range of resources used and time taken including activities, magazines, DVD and numerous other options.</p> <p>Arm 2 (control): No education.</p>	<p>A baseline questionnaire was completed by the control group only but not the intervention group.</p> <p>A second questionnaire was completed by both groups 6 months post-intervention.</p> <p>Semi-structured focus groups and interviews were also conducted with both groups.</p>	<p>1. Statistically significant difference between groups with increased HPV and vaccination knowledge in intervention group.</p> <p>2. Improved sexual intentions in intervention group.</p> <p>3. No change in HPV vaccination uptake.</p> <p>4. While falling slightly, knowledge remained high in the intervention group 6 months post-intervention.</p>

Lim et al. 2017 (Singapore)	Quasi-experimental Pre-test/Post-test with 1 group only	1. To assess knowledge and attitudes towards cervical cancer, human papillomavirus and the HPV vaccination before and after the intervention.	<i>Age:</i> 15-19 years (99.3%) <i>Gender:</i> Female only <i>Numbers:</i> 150 students (1 junior college only) One of the top pre-university centres in Singapore so may not be very representative of the whole population.	Not discussed	<i>Intervention:</i> a presentation on individual tablets with no evidence of any discussion with the team members after the presentation. Delivered by trained members of the research team though unclear Q&A opportunity. Intervention lasted 10 minutes on average.	A baseline questionnaire was completed. A second post-intervention questionnaire was completed directly after the intervention.	1. The intervention resulted in raised awareness and knowledge in most aspects with regards to HPV, HPV vaccine and Pap smears to prevent cervical cancer. 2. Increased intention to be vaccinated was also found after the intervention.
Yoost et al. 2017 (USA)	Quasi-experimental Pre-test/Post-test with 1 group only	1. To evaluate the use of telehealth as a tool for teaching reproductive health. 2. To evaluate changes in student knowledge and	<i>Age:</i> Average 16.1 (range 14-18 years) <i>Gender:</i> Females only <i>Numbers:</i> 26 students completed the initial pre and	Not discussed	<i>Intervention:</i> A 1 hour after school telehealth session detailing types of STDs and modes of transmission, long-term complications, prevention of	Pre- and post-intervention questionnaires were completed at each session and were used to assess subject knowledge	1. A statistically significant change in knowledge was seen regarding human papillomavirus (HPV) and vaccination knowledge after the intervention.

		self-efficacy after the telehealth intervention.	post test questionnaires but only 21 completed the 6 month questionnaire from 2 secondary/ high schools		<p>STDs, condom use, and HPV vaccination. Review of local resources for obtaining condoms and STD testing.</p> <p>Taught by a team of faculty, residents, or medical students based out of a medical school.</p> <p>All sessions were conducted using interactive real-time teleconferencing</p> <p>An online portal enabled students to ask anonymous questions which were answered during the following session.</p>	<p>and self-efficacy.</p> <p>6 months after the telehealth program, students completed a follow-up questionnaire to reassess knowledge and self-efficacy measures..</p>	<p>2. HPV vaccine initiation or completion was 38% (10/26) at the time of the intervention session. This report increased to 71.4%, 15/21 at 6 months among those who attended that session.</p> <p>3. Personal attitudes and beliefs about STD prevention showed a positive trend at the 6-month evaluation, but did not reach statistical significance.</p> <p>4. At 6 months, 81% (30/37) reported “confident” or “very confident” on a Likert scale, that they could obtain condoms if needed, compared with 85.7% (24/28) at pre-test (P = .45)</p>
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					Financial incentives were offered for participation.		
Grandahl et al. 2016 (Sweden)	2-armed Cluster RCT	1. To improve primary prevention of HPV by promoting HPV vaccination and increased condom use.	<p><i>Age:</i> 16 years only.</p> <p><i>Gender:</i> Males and Females</p> <p><i>Numbers:</i> 18 schools (751 students recruited with 741 completing the study)</p>	<p>-Health Belief Model (HBM)</p> <p>-The Theory of Reasoned Action (TRA)</p>	<p>Arm 1 (intervention): School nurses delivered a face-to-face 30 minute individual structured and consistent interview.</p> <p>Arm 2: no structured teaching</p>	<p>A baseline questionnaire was completed pre-intervention and a second questionnaire was completed 3 months post-intervention.</p> <p>(authors indicated that FU may be done at 12 and 24 months though results not published here)</p>	<p>1. The intervention had a significant positive effect on intention to use condoms ($p=0.004$).</p> <p>2. The intervention had a significant positive effect on HBM score ($p=0.003$), with a 2.559 points higher score for the intervention group.</p> <p>3. HPV vaccination rates increased to a higher degree compared to the control group ($p=0.02$)</p> <p>4. There were no significant differences between the intervention and the control groups regarding their reports of actual condom use during their latest act</p>

							of intercourse (p=0.377).
Lai et al. 2015 (Taiwan)	A quasi-experimental 2-armed study	1. To identify the effectiveness of a Facebook-assisted teaching method for a school-based intervention on knowledge and attitudes about cervical cancer prevention and on HPV vaccination intention.	<p><i>Age:</i> 15-17 years old</p> <p><i>Gender:</i> Females only</p> <p><i>Numbers:</i> 1 school (200 students)</p> <p>(4 classes selected out of 16 classes)</p>	- Health Belief Model (HBM)	<p>All 200 participants had a 50 min lecture with brief discussion delivered by a nursing teacher.</p> <p>Arm 1 (intervention): Over the next 2 weeks this 100 students then had the option of entering facebook discussions.</p> <p>Arm 2 (control): Over the next 2 weeks this 100 students then had the option of entering face-to-face discussions.</p> <p>72 out of 100 attended facebook discussions but no indication of</p>	<p>A baseline questionnaire was completed by all students pre-education</p> <p>A second questionnaire was completed 2 weeks post-lecture.</p> <p>A third questionnaire was completed 8 weeks post-lecture.</p>	<p>1. Knowledge, attitude and intention to vaccinate were all better in the intervention arm though improvements were noted in both arms from baseline.</p> <p>2. The intervention group outcomes remained significantly higher than those in the control group at least 8 weeks after the lecture.</p>

					number of students who engaged in face-to-face discussions.		
Gargano et al. 2014 (USA)	Quasi-experimental 3-armed study	1. To increase adolescent vaccination rates 2. To assess changes in knowledge and attitudes towards HPV vaccination after participating in the intervention	<i>Age:</i> 11-18 years old <i>Gender:</i> Females only <i>Numbers:</i> 15 schools (1068 students)	-Health Belief Model (HBM)	Arm 1 (control): no intervention Arm 2: Approx. 120 minutes over 2-3 days with a variety of interactive activities but done consistently. Science Teachers delivered the education. A specially constructed brochure was also sent to parents who participated in Arm 2. Arm 3: Parent directed brochure only.	A baseline questionnaire was completed pre-intervention and a second questionnaire was completed 3 days post-intervention.	1. The intervention group (Arm 2) showed an increase in interest in receiving HPV vaccine post-intervention. 2. The intervention group (Arm 2) showed improved knowledge and attitudes relating to HPV vaccination post-intervention (p<0.001).

Steckelberg et al. 2013 (Germany)	2-armed RCT	1. To compare the effects of an information leaflet including numerical data to standard information without numerical data on 'risk knowledge' regarding HPV vaccination in disadvantaged school girls of full-time vocational schools.	<i>Age:</i> 15-22 years old <i>Gender:</i> Females only <i>Numbers:</i> 3 schools (105 students)	Not discussed.	<p>Arm 1 (intervention arm): standard leaflet was supplemented with numerical information on cancer risk and on benefit of the HPV vaccination in terms of cancer prevention.</p> <p>(No actual teaching delivered though students were in class for a 90 minute period to review leaflets.)</p> <p>Arm 2: Standard HPV information leaflet.</p> <p>After each intervention, participants had Q&A and discussion opportunity.</p>	A baseline questionnaire was completed pre-intervention and a second questionnaire was completed directly after the intervention.	1. Risk knowledge was better in the modified leaflet group (intervention group).
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Marek et al. 2012 (Hungary)	Quasi-experimental 2-armed study	1. To establish the impact of a school-based HPV-focused intervention on adolescents' knowledge, beliefs and attitudes towards the prevention of HPV infection and cervical cancer 3-months following the program.	<i>Age:</i> 14-19 years old <i>Gender:</i> both males and females <i>Numbers:</i> 2 schools (394 completed baseline questionnaire and 378 completed 3 month post-test questionnaire but they may not be the same students 191 students attended the intervention in total.	Not discussed	One school was the control and other school the intervention. Arm 1 (intervention): A trained health educator (1 st author) delivered the intervention. Education in 8 classes (25-33 students in each class). 45 min didactic presentation followed by Q&A and handouts. Arm 2 (control) : No education provided.	Both groups conducted baseline questionnaires and a second questionnaire 3 months after the intervention.	1. Results confirm that female students had higher baseline knowledge of HPV and cervical cancer compared to males. 2. Both genders in the intervention group demonstrated significant improvement in knowledge, attitude and intention to be vaccinated despite financial barriers in comparison to the control group.
Merzouk et al. 2011 (USA)	2-armed RCT	1. To assess baseline and post-intervention knowledge of HPV.	<i>Age:</i> Not stated but likely 14-18 years old. <i>Gender:</i> Not stated but	Not discussed.	Arm 1 (intervention): 15 minute HPV DVD educational intervention plus standard health class	Questionnaire at baseline (pre-education) and directly after intervention.	1. Improvement in knowledge was significantly better in the DVD (intervention) group (P < .0001) compared to the control group.

			possibly females only as information is generally focused on cervical cancer <i>Numbers:</i> 626 participants completed the study		scheduled over 2 days. Content of DVD is not very clear. Arm 2: Control. Standard health class only (Health classes were delivered by teachers.)		
Kwan et al. 2011 (Hong Kong)	Quasi-experimental Pre-test/Post-test with 1 group only	To evaluate the effects of a school-based cervical cancer education intervention on; 1. knowledge, attitude and perceived social norms towards HPV vaccination. 2. students' intention to be vaccinated.	<i>Age:</i> 12-17 years old <i>Gender:</i> Females only <i>Numbers:</i> 4 schools (953 students completed the study)	- Theories of persuasion	<i>Intervention:</i> Didactic slide presentation delivered by a gynecological oncologist followed by an interactive Q&A session lasting 1hr in total. (large groups ranging from 179 to 426 girls) Information sheet provided prior to teaching session.	A baseline questionnaire was completed pre-intervention and a second questionnaire was completed directly after the intervention.	1. Increase in knowledge, more positive attitude towards HPV vaccination and increased perceived support from family and peers were evident after the intervention. 2. More students indicated a positive intention to accept the vaccine after the intervention.

<p>Gottvall et al. 2010</p> <p>(Sweden)</p>	<p>A quasi-experimental 2-armed study.</p>	<p>1. To evaluate the effect of an educational intervention about HPV and preventive methods for cervical cancer, such as vaccination, condom use and Pap smear testing on knowledge of HPV and attitudes to preventive methods.</p>	<p><i>Age:</i> Mean age 16 years though the range was not stated but all in 1st year of high school</p> <p><i>Gender:</i> both males and females</p> <p><i>Numbers:</i> 6 schools (276 students)</p> <p>(A strategic sample of first year students from both vocational and theoretical high school programmes)</p>	<p>- Health Belief Model (HBM)</p>	<p>2 control groups to assess whether pre intervention questionnaire affected outcome.</p> <p>Arm 1 (intervention): A Registered nurse (who was also one of the research authors) delivered a 1 hr lesson plan (20 mins lecture, condom demonstration and practice, wrap-up discussion and take away folder with link to website to complete activities)</p> <p>Arm 2+3 (controls): No lesson plan</p>	<p>A baseline questionnaire was completed by all students pre-intervention and a second questionnaire was completed directly after the intervention.</p>	<p>1. At follow-up, the median knowledge score had significantly increased in the intervention group but not in the comparison group ($P < 0.001$).</p> <p>2. Attitudes to HPV vaccination, condom use and Pap smear testing remained the same ($P > 0.05$). This may be due to a positive baseline attitude.</p>
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<p>Lloyd et al. 2009</p> <p>(UK)</p>	<p>A quasi-experimental 3-armed study.</p>	<p>1. To assess effect of HPV information on knowledge and anxiety.</p> <p>2. To assess future intentions to participate in cervical screening, HPV testing, and HPV vaccination after this intervention.</p>	<p><i>Age:</i> 13-16 years old</p> <p><i>Gender:</i> Female only</p> <p><i>Numbers:</i> 2 schools with 174 students recruited (2 of these students were excluded)</p>	<p>- Leventhal's Common Sense Model of lay illness representations.</p>	<p>Arm 1 (intervention): Leaflet with HPV, Chlamydia and environmental information</p> <p>Arm 2 (control): Leaflet with Chlamydia information only</p> <p>Arm 3 (control): Leaflet with environmental information only.</p> <p>Students were given 5 minutes to read each leaflet.</p>	<p>No baseline questionnaire was provided.</p> <p>Questionnaire was completed directly after reading the leaflets.</p> <p>Knowledge was assessed using true or false statements about HPV, and anxiety using the six-item State-Trait Anxiety Inventory (STAI).</p>	<p>1. The Intervention group demonstrated significantly more HPV knowledge ($p < .001$) than controls post-intervention.</p> <p>2. Intentions to attend cervical screening and accept HPV vaccination were highest in intervention group intentions</p> <p>3. Intentions to have HPV testing were equally high in all groups.</p>
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Table 1: Study Properties

